WHAT IS CLAIMED IS:

12 hab

#:# #:#

The state of the s

‡:<u>;</u>

29. A tissue adhesive based on fibrinogen, said tissue adhesive comprising an admixed elastase inhibitor.

- 30. A tissue adhesive as set forth in claim 29, wherein said elastase inhibitor is selected from the group consisting of eglin, elastase-al-proteinase inhibitor, al-antiprotease, leukocyte protease inhibitor, elafin and mixtures thereof.
- 31. A tissue adhesive as set forth in claim 30, wherein said leukocyte protease inhibitor is provided as a leukocyte fraction.
- 32. A tissue adhesive as set forth in claim 31, wherein said leukocyte fraction is a granulocyte-derived fraction.



- 33. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is comprised of human proteins.
- 34. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is comprised of human blood proteins.
- 35. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is comprised of human plasma proteins.

A tissue adhesive as set forth in claim 29, wherein said elastase inhibitor is contained in an amount ratio of from 1:100 to 1:150,000, based on milligrams of fibrinogen.

- 37. A tissue adhesive as set forth in claim 29, wherein the amount of said elastase inhibitor to fibrogen in a ratio of from 1:500 to 1:110,000.
- 38. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive contains at least 10⁻⁶ U of elastase inhibitor per gram of fibrinogen.

- A tissue adhesive as set forth in claim 29, wherein said tissue adhesive contains from 39. between 10⁻³ and 10 U of elastase inhibitor per gram of fibrinogen.
- A tissue adhesive as set forth in claim 29, further comprising plasminogen in an 40. amount of at least 0.0001 mg/mg of fibrinogen.

- A tissue adhesive as set forth in claim 40, wherein said plasminogen is contained in 41. an amount of at least 0.001 mg/mg of fibrinogen.
- A tissue adhesive as set forth in claim 40, wherein said plasminogen is contained in 42. an amount of more than 0.01 mg/mg of fibrinogen.
- A tissue adhesive as set forth in claim 29, wherein said tissue adhesive does not contain any plasminogen.
- A tissue adhesive as set forth in claim 29, further comprising at least one of a plasmin 44. inhibitor and a plasmin activator inhibitor.
- A tissue adhesive as set forth in claim 44, wherein said at least one of said plasmin 45. inhibitor and said plasmin activator inhibitor is selected from the group consisting of aprotinin, α_2 -macroglobulin, α_1 -antitrypsin, ϵ -aminocaproic acid, tranexamic acid and mixtures thereof.
- A tissue adhesive as set forth in claim 29, further comprising an antibiotic. 46.
- A tissue adhesive as set forth in claim 46, wherein said antibiotic is selected from the 47. group consisting of aminoglycosides, betalactams, polypeptides, fosfomycin, tetracyclins and mixtures thereof.



48. A tissue adhesive as set forth in claim 29, further comprising factor XIII.

- 49. A tissue adhesive as set forth in claim 48, wherein said factor XIII is contained in an amount of at least 0.001 U/mg of fibrinogen.
- 50. A tissue adhesive as set forth in claim 48, wherein said factor XIII is contained in an amount of at least 0.1 U/mg of fibrinogen.
- 51. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is free from kininogenic proteins.
- 52. A tissue adhesive as set forth in claim 29, further comprising a solid surface, said tissue adhesive being present as a fleece in combination with said solid surface.

7

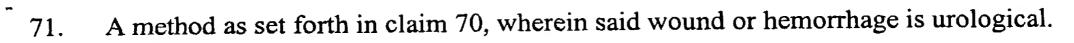
53. A tissue adhesive as set forth in claim 52, wherein said solid surface is selected from the group consisting of a collagen surface, a gelatin surface and a polysaccharide surface.

SP.

- 54. A tissue adhesive set forth in claim 29, wherein said tissue adhesive is resistant to lysis in an environment with high fibrinolytic activity for a period of time which is at least 10 hours.
- 55. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is resistant to lysis in an environment with high fibrinolytic activity for a period of time which is at least 15 hours.
- 56. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is lyophilized.
- 57. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is present in solution.
- 58. A tissue adhesive as set forth in claim 57, wherein said solution is deep-frozen.
- 59. A tissue adhesive as set forth in claim 29, wherein said tissue adhesive is present in virus-inactivated form.

- 60. A tissue adhesive as set forth in claim 29, wherein said elastase inhibitor is of recombinant origin.
- 61. A tissue adhesive system comprising fibrinogen and an elastase inhibitor.
- 62. A tissue adhesive system as set forth in claim 61, further comprising a thrombin-containing component.
- 63. A tissue adhesive system as set forth in claim 62, wherein said thrombin-containing component further comprises calcium.
- 64. A tissue adhesive system comprising a fibrinogen component and an elastase-inhibitor-containing component.
- 65. A tissue adhesive system as set forth in claim 64, wherein said elastase-inhibitor-containing component contains thrombin.
- 66. A tissue adhesive system as set forth in claim 61, further comprising an application device for said at least one component.
- 67. A tissue adhesive system as set forth in claim 66, wherein said application device is a double-syringe system.
- 68. A tissue adhesive system as set forth in claim 64, further comprising an application device for said fibrinogen component and for said elastase-inhibitor containing component.
- 69. A tissue adhesive system as set forth in claim 68, wherein said application device is a double-syringe system.
- 70. A method for treating wounds or hemorrhages with high fibrinolytic activity in patients, comprising administering an effective dose of a tissue adhesive preparation containing fibrinogen and an elastase inhibitor.





- 72. A method for treating wounds or hemorrhages in patients, comprising administering an effective dose of a tissue adhesive containing fibrinogen and an elastase inhibitor by means of an application device.
- 73. A method as set forth in claim 72, wherein said wound or hemorrhage is urological. ---

Date: <u>February 28, 2000</u>

the state and state is a self-state with

Įij.

House though them therefore through thems

Patent Group One Post Office Square Boston, Massachusetts 02109 Telephone: (617) 832-1294 Facsimile: (617) 832-7000 Respectfully submitted, Foley, Hoag & Eliot, LLP

Beth E. Arnold Registration No. 35,430 Attorney for Applicant

384890